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File No. 16051-7US CC/DBB/

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Andrew VAILLANT et al.  
Serial Number: 10/661,402  
Filing Date: September 12, 2003  
For: ANTIVIRAL OLIGONUCLEOTIDES TARGETING VIRAL  
FAMILIES  
Art Unit: 1648  
Examiner: HURT, Sharon L.  
Agent: Cawthorn, Christian

DECLARATION UNDER 37 C.F.R. SEC. 1.132

I, Jean-Marc Juteau, do hereby declare and state as follows:

1. I received the degrees of Bachelor (B.Sc.) of Biology from Montreal University in 1985, Master (M.Sc.) of Microbiology and Immunology from Montreal University in 1988, and Doctor of Philosophy (Ph.D.) of Microbiology and Immunology from Laval University in 1991.
2. My academic background and experiences in the field of the present invention are listed on the enclosed *curriculum vitae*.
3. I am a founder since 1999 of REPLICor Inc. and Senior Vice President since 2002.
4. I am an author of several scholarly publications as listed in my enclosed *curriculum vitae*.

5. I am an inventor in the present application; I have read and am thoroughly familiar with the contents of U.S. Patent Application Serial No. 10/661,402 entitled "ANTIVIRAL OLIGONUCLEOTIDES TARGETING VIRAL FAMILIES", including the claims.
6. I have also read and understood the latest Official Action from the PTO dated March 10, 2006. In this Office Action, claims 52-56 were rejected for lack of enablement under 35 U.S.C. §112, first paragraph.
7. The following experiments had been performed in the period between September 2003 to July 2006 under the supervision of Andrew Vaillant (inventor on this invention) and myself, by contractors or collaborators, to obtain results for antiviral activity of sequence independent oligonucleotides of the present invention against several different viruses. All contractors or collaborators executed these standard assays following strict instructions from Andrew Vaillant or myself. These *in vitro* and one *in vivo* assays of viral infection are standard assays that can be used for the demonstration of a drug activity. These assays cover different viruses, different viral families, different strains, RNA and DNA viruses.

The following experiments were conducted to evaluate the antiviral activity of sequence independent oligonucleotides against a variety of viruses.

Family	Virus	Strain (resistance)	Assay	REP 2006 IC <sub>50</sub> (uM)
Orthomyxoviridae	Influenza A	A/Vietnam/1203/04 [H5N1]	CPE / Hemagglutination	<0.6 (duplicated)
		R292K- A/Sydney/05/97 [H3N2] Tamiflu™ resistant Relenza™ resistant	CPE	<0.1 (Tamiflu > 64uM)
		New Caledonia [H1N1]	CPE	0.014
		Taiwan [H1N1]	CPE / Hemagglutination	0.014
		PR8 [H1N1]	CPE / Hemagglutination	0.055
		Hong Kong/68 [H3N2]	CPE / Hemagglutination	0.008
		WSN [H3N2]	CPE / Hemagglutination	0.038
		New Caledonia/20/99* [H1N1]	CPE	<0.05
		Texas [H1N1]	CPE	< 0.05
		Sydney/5/97 [H3N2]	CPE	<0.05 (Tamiflu = 0.64uM)
		Panama/2007/99* [H3N2]	CPE	<0.05
	Influenza B	E119G- B/Beijing/1/87 Tamiflu™ resistant Relenza™ resistant	CPE	3.12 (Tamiflu ~320uM)
		Harbin/7/94	CPE	<0.05
		Panama	CPE / Hemagglutination	0.038
		Singapore	CPE / Hemagglutination	0.038
Paramyxoviridae	Human Metapneumo	P10	CPE / Hemagglutination	Active /not quantified
		26575	CPE / Hemagglutination	Active /not quantified
		RLBx	CPE / Hemagglutination	Active /not quantified
Herpesviridae	Varicella Zoster	Ellen	CPE	<0.02
	Epstein-Barr Virus	P3H-R	DNA Hybridization	14.7
	HHV-6A	GS	DNA Hybridization	10.2

Family	Virus	Strain (resistance)	Assay	REP 2006 IC <sub>50</sub> (uM)
	HHV-6B	Z29	DNA Hybridization	2.9
Retroviridae	Friend's Leukemia Virus		In vivo (reduction of CD34+ splenocytes by FACS)	10mg/kg/10 days SC 68% reduction
Filoviridae	Ebola	Zaire Mayinga	Fluorescent PRA, CPE and Ebola-GFP FACS	0.03
	Marburg	Musoke	Fluorescent PRA	IC99 < 1
Arenaviridae	Lassa Fever	Josiah	Fluorescent PRA	IC99 < 1
	Lymphocytic Choriomeningitis	clone 13	CPE	~0.1
	Lymphocytic Choriomeningitis	ARM53b	CPE	~0.1
	Guanarito		CPE	~0.3
	Junin		CPE	~1
	Machupo		CPE	~0.2
Orthopoxviridae	Mousepox (ectromelia)		CPE	0.4
Rhabdoviridae	Rabies	Evelyn Rudnick	CPE	IC99 < 1uM
Bunyaviridae	Rift Valley Fever		CPE	< 1uM
	Crimean Congo Hemorrhagic Fever		CPE	Active but not quantified
Flaviviridae	Hepatitis C	JFH1	Fluorescent PRA	>100nM (infectious in vitro model) (REP 2031 >100nM as well)
	West Nile	NY-99	CPE	3.02
	Yellow Fever	17D	CPE	3.47
	Dengue	Serotype 1	CPE	~10
	Tick born encephalitis		Fluorescent detection of infection	Active but not quantified
Togaviridae	Western Equine Encephalitis		CPE	0.156

Family	Virus	Strain (resistance)	Assay	REP 2006 IC <sub>50</sub> (uM)
Rhabdoviridae	Vesicular stomatitis	Indiana	CPE	-70
	Rabies	Evelyn Rudnick	CPE	IC99 < 1uM
Coronaviridae	Mouse Hepatitis	A59	Fluorescent plaque detection	Active but not quantified
	Human Corona	OC43	Fluorescent plaque detection	Active but not quantified

Abbreviations: CPE, cytopathic effect; PRA, plaque reduction assay ; GFP, green fluorescent protein ; FACS, Fluorescence-activated cell sorter.

8. The results presented hereinabove and produced according to the teaching disclosed in the U.S. Patent Application Serial No. 10/661,402, clearly proves that that the present invention covers broad spectrum antiviral oligonucleotides. In the application, the antiviral activity of HIV-1, HIV-2, HSV-1, HIV-2, RSV, parainfluenza virus and HBV and of other viruses from 4 different families, namely Coxsackie virus B2, vaccinia virus, hantavirus and parainfluenza-3 virus clearly predicted the activity in other families of viruses as demonstrated in this declaration. Indeed, the antiviral activity of the sequence independent oligonucleotides of the present invention is demonstrated in a "representative number of species", in all, 28 different viruses from 13 families.

9. I hereby declare that all statements made herein of my own knowledge are true, and that all statements made on information and belief are believed to be true, and that these statements were made with the knowledge that willful false statements and the like so made are punishable by a fine or imprisonment, or both (18 U.S.C. Sec. 1001), and may jeopardize the validity of the application of any patent issuing thereon.

Signed



Jean-Marc Juteau

Dated: September 9, 2006

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**Curriculum vitae****JEAN-MARC JUTEAU, Ph.D**

Address: 66 de Vincennes  
Blainville, QC  
Canada  
H7B 1W7

Telephone: (450) 434-8932 (home)  
(450) 688-6068 (work)

Age: 42

Status: Married, three kids

Language spoken and written: French and English

**EXPERIENCE****01-2002 - today**

**Senior Vice-President and Founder, REPLICor Inc., Laval.**  
Biopharmaceutical company developing antiviral and anticancer drugs.

**Responsibilities:**

- Science development.  
*Day to day contact with CSO, scientific input.*
- In charge of intellectual property portfolio.  
*Patent writing, strategy, management.*

**02-1999 – 01-2002**

**CEO and founder, REPLICor Inc., Laval.**

**Responsibilities:**

- Science development
- In charge of financing  
*Instrumental in raising \$2.5M in equity and loan*
- In charge of licensing and contract agreement  
*Negotiation of licenses and contracts with universities*

**02-1996 to 02-1999**

**Officer, Office of Technology Transfer, McGill University, Montreal.**

**Responsibilities:**

- Agreement management and negotiation  
*License, research, option, confidentiality, material distribution.*
- Spin-off company projects  
*Set-up of spin-off company, contact with investors, business plan.*

**03-94 to 02-96**

**Product Manager, Iso Tech Design, Laval**

Company developing and marketing micro-environments for pharma applications.

**Responsibilities:****CONFIDENTIAL**

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- Microbiology quality control..
- Distributor formation

*Contacts: Baxter Health Care, VWR, Khulman Tech., E.S.I. FluFrance, Liberty Clean Rooms, Millipore.*

91 à 10-93

**Director and Co-founder, DIAGNOGENE inc., R&D in biotechnology, Ste-Foy**  
Responsibilities: Financial and research administration, representation.

**RESEARCH TRAINING**09-92 à 11-93

Post-doctoral scientist, **INRS-santé, Pointe-Claire**  
Project: In-vitro mutagenesis of 4-chlorobenzoate dehalogenase in *Pseudomonas sp.* CBS3.

08-91 à 09-92

Post-doctoral scientist, **Institut de Recherches Cliniques de Montréal**  
Project: Cloning et characterization of a cardiac specific transcription factor.

11-90

Training in molecular modeling, Department of Molecular and Cell Biology, **University of Connecticut.**

05-88 to 06-88

Workshop on DNA technologies: Sequence and in-vitro mutagenesis, **University of North-Carolina, Chapel Hill, NC.**

**EDUCATION**87-91

Doctorate (Ph.D.), Microbiology and Immunology, **Laval University.**  
Molecular biology, epidemiology and structure-function analysis of the ROB-1  $\beta$ -lactamase.

85-87

Master (M.Sc.), Microbiology and Immunology, **Montreal University and Hôtel-Dieu Hospital.**  
Granulocytar function in recurrent vaginitis.

82-85

Bachelor (B.Sc.), Biology, **Montreal University.**

**BOARD MEMBERSHIP**2005- today

Member of the Montreal Life Science Committee.

2004- today

President of the Alumni Association of Montreal Clinical Research Institute.

**SCHOLARSHIP, AWARD and PRIZES**

Industrial Design Prize 1995 from the Design Institute (received in team for a micro-environment)  
Institut National de la Recherche Scientifique (INRS) Fellowship, 1992-93.  
Medical Research Council (MRC) Fellowship, 1992.  
Fonds de la Recherche en Santé du Québec (FRSQ) Studentship, 1989-90-91.  
Fonds pour la Formation des Chercheurs et l'Aide à la Recherche (FCAR) Studentship, 1988-89.  
Canlab Prize from l'Association des Microbiologistes du Québec, 1989.

**CONFIDENTIAL**



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**AUTHORSHIP**

Patent filings: 20  
Scientific articles: 10  
Posters and oral presentations: 30

Vaillant A, Juteau JM, Lu H, Liu S, Lackman-Smith C, Ptak R, Jiang S. Phosphorothioate oligonucleotides inhibit human immunodeficiency virus type 1 fusion by blocking gp41 core formation. *Antimicrob Agents Chemother*. 2006 Apr;50(4):1393-401.

Kocisko DA, Vaillant A, Lee KS, Arnold KM, Bertholet N, Race RE, Olsen EA, Juteau JM, Caughey B. Potent antiscrapie activities of degenerate phosphorothioate oligonucleotides. *Antimicrob Agents Chemother*. 2006 Mar;50(3):1034-44.

Moaddel R, Price GB, Juteau JM, Leffak M, Wainer IW. The synthesis and initial characterization of an immobilized DNA unwinding element binding (DUE-B) protein chromatographic stationary phase. *J Chromatogr B Analyt Technol Biomed Life Sci*. 2005 Jun 25;820(2):197-203.

Sylvestre M, Sirois M, Hurtubise Y, Bergeron J, Ahmad D, Shareck F, Barriault D, Guillemette I, Juteau JM. Sequencing of *Comamonas testosteroni* strain B-356-biphenyl/chlorobiphenyl dioxygenase genes: evolutionary relationships among Gram-negative bacterial biphenyl dioxygenases. *Gene*. 1996 Oct 3;174(2):195-202.

Ahmad D, Fraser J, Sylvestre M, Larose A, Khan A, Bergeron J, Juteau JM, Sondossi M. Sequence of the bphD gene encoding 2-hydroxy-6-oxo-(phenyl/chlorophenyl)hexa-2,4-dienoic acid (HOP/cPDA) hydrolase involved in the biphenyl/polychlorinated biphenyl degradation pathway in *Comamonas testosteroni*: evidence suggesting involvement of Ser112 in catalytic activity. *Gene*. 1995 Apr 14;156(1):69-74.

Juteau JM, Billings E, Knox JR, Levesque RC. Site-saturation mutagenesis and three-dimensional modelling of ROB-1 define a substrate binding role of Ser130 in class A beta-lactamases. *Protein Eng*. 1992 Oct;5(7):693-701.

Maclean IW, Slaney L, Juteau JM, Levesque RC, Albritton WL, Ronald AR. Identification of a ROB-1 beta-lactamase in *Haemophilus ducreyi*. *Antimicrob Agents Chemother*. 1992 Feb;36(2):467-9.

Juteau JM, Cote S, Levesque RC. Systematic site-saturation mutagenesis of ROB-1 beta-lactamase: efficiency of T4 polymerase and oligonucleotide synthesis. *Biotechniques*. 1991 Oct;11(4):460-2.

Juteau JM, Sirois M, Medeiros AA, Levesque RC. Molecular distribution of ROB-1 beta-lactamase in *Actinobacillus pleuropneumoniae*. *Antimicrob Agents Chemother*. 1991 Jul;35(7):1397-402.

Juteau JM, Levesque RC. Sequence analysis and evolutionary perspectives of ROB-1 beta-lactamase. *Antimicrob Agents Chemother*. 1990 Jul;34(7):1354-9.

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